

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |  |
|---|--|--|
| Applicant's or agent's file reference<br><b>10104SG281</b>  | <b>FOR FURTHER ACTION</b> <div style="text-align: right;">see Form PCT/ISA/220<br/>as well as, where applicable, item 5 below.</div> |  |
| International application No.<br><b>PCT/SG2005/000051</b>   | International filing date (day/month/year)<br><b>21 February 2005</b>  | (Earliest) Priority Date (day/month/year)<br><b>25 February 2004</b> |
| Applicant<br><b>NATIONAL UNIVERSITY OF SINGAPORE et al.</b> |  |  |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

#### Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.
2. ☒ Certain claims were found unsearchable (See Box No. II).
3. ☐ Unity of invention is lacking (See Box No. III).
4. With regard to the title,
 

☒ the text is approved as submitted by the applicant.  
☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
 

☒ the text is approved as submitted by the applicant.  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the drawings,
  - a. the figure of the drawings to be published with the abstract is Figure No.
 

☐ as suggested by the applicant.  
☐ as selected by this Authority, because the applicant failed to suggest a figure.  
☐ as selected by this Authority, because this figure better characterizes the invention.
  - b. ☒ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2005/000051

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-24, 29, 56, 57 (in part)  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
A complete search of claims 1-24, 29, 56 and 57 was not feasible for economic reasons. Consequently the search was based on methods for predicting crystallisation conditions as exemplified in the specification.
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2005/000051

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. <sup>7</sup>: C07K 14/42, 14/435, 14/765.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See electronic database consulted below.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 STN (File Medline, CA, WPIDS, Biosis); Keywords: crystalli?, surface(w)pressure, surface(w)tension, protein, nucleic(w)acid, virus, dna, rna, lysozyme, bsa, bovine(w)serum(w)albumin, concanavalin(w)a, concalavinc(w)a

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| A         | CURTIS, R. A. et al., Hydrophobic Forces Between Protein Molecules in Aqueous Solutions of Concentrated Electrolyte, Biophysical Chemistry (2002), 98, 249-265. | 1-57                  |
| A         | AGENA, S. M. et al., Protein Solubility Modeling, Biotechnology and Bioengineering, (1999), 64(2), 144-150.   | 1-57                  |



Further documents are listed in the continuation of Box C



See patent family annex

|     |   |     |  |
|-----|---|-----|--|
| "A" | Special categories of cited documents:<br>document defining the general state of the art which is not considered to be of particular relevance                      | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "E" | earlier application or patent but published on or after the international filing date   | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" | document referring to an oral disclosure, use, exhibition or other means  | "&" | document member of the same patent family  |
| "P" | document published prior to the international filing date but later than the priority date claimed  |     |  |

Date of the actual completion of the international search

16 March 2005

Date of mailing of the international search report

29 MAR 2005

Name and mailing address of the ISA/AU

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# PATENT COOPERATION TREATY

From the:  
INTERNATIONAL SEARCHING AUTHORITY

To:

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P.O. Box 1531  
Robinson Road Post Office  
Singapore 903031

## PCT

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) 29 MAR 2005

Applicant's or agent's file reference  
10104SG281

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/SG2005/000051

International filing date (day/month/year)  
21 February 2005

Priority date (day/month/year)  
25 February 2004

International Patent Classification (IPC) or both national classification and IPC  
Int. CL<sup>7</sup> C07K 14/42, 14/435, 14/765.

Applicant  
NATIONAL UNIVERSITY OF SINGAPORE et al.

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application  |

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU  
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**MARIE-ANNE FAM**  
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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

**PCT/SG2005/000051**

**Box No. I      Basis of the opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SG2005/000051

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 1-24, 29, 56, 57 (in part)

because:

- ☐ the said international application, or the said claim Nos.  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-24, 29, 56, 57 (in part)

are so unclear that no meaningful opinion could be formed (*specify*):

A complete search of claims 1-24, 29, 56 and 57 was not possible for economic reasons. Consequently this opinion is based only on methods for predicting crystallisation conditions in so far as covered by the search.

- ☐ the claims, or said claims Nos.  
are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/SG2005/000051

**Box No. V** Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**1. Statement**

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Claims 1-57 | YES |
|                               | Claims -    | NO  |
| Inventive step (IS)           | Claims 1-57 | YES |
|                               | Claims -    | NO  |
| Industrial applicability (IA) | Claims 1-57 | YES |
|                               | Claims -    | NO  |

**2. Citations and explanations:**

**Novelty and Inventive Step**

The following documents were identified in the International Search Report:

D1 Biophysical Chemistry

D2 Biotechnology and Bioengineering

The present invention relates to methods for predicting crystallisation conditions for proteins and the like. Current methods for determining these conditions usually employ the second virial coefficient  $B_{22}$ . However this coefficient is based only on intermolecular interactions and hence does not always provide reliable results.

In contrast, the present invention uses methods that are based on both intermolecular interactions and kinetic effects. This enables protein crystallisation conditions to be predicted with greater reliability. Neither D1 nor D2 discloses methods as defined by the present claims. Consequently claims 1-57 are considered novel and inventive over the prior art.

**Industrial Applicability**

Claims 1-57 meet the requirements for industrial applicability.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

**PCT/SG2005/000051**

**Box No. VIII    Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claims 1 and 29 are not fully supported by the description. The claims are directed to methods for crystallising macromolecules which involve the monitoring of an assembly parameter. According to the specification, this parameter may be one of density, conductivity, detergency and the like. However, the description only provides support for methods wherein the surface pressure or surface tension is chosen as the assembly parameter. It has not been demonstrated that crystallisation conditions may be accurately predicted when other assembly parameters are employed.